Lifetime Risk of Blindness in Open-Angle Glaucoma

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• PURPOSE: **To determine the lifetime risk and duration of blindness in patients with manifest open-angle glaucoma (OAG).**
• DESIGN: **Retrospective chart review.**
• METHODS: **We studied glaucoma patients who died between January 2006 and June 2010. Most glaucoma patients living in the catchment area (city of Malmö; n = 305 000) are managed at the Department of Ophthalmology at Skåne University Hospital in Malmö. From the patient records we extracted visual field status, visual acuity, and low vision or blindness as defined by the World Health Organization (WHO) criteria and caused by glaucoma at the time of diagnosis and during follow-up. We also noted age at diagnosis and death and when low vision or blindness occurred.**
• RESULTS: **Five hundred and ninety-two patients were included. At the time of the last visit 250 patients (42.2%) had at least 1 blind eye because of glaucoma, while 97 patients (16.4%) were bilaterally blind, and 12 patients (0.5%) had low vision. Median time with a glaucoma diagnosis was 12 years (<1-29), median age when developing bilateral blindness was 86 years, and median duration of bilateral blindness was 2 years (<1-13). The cumulative incidences of blindness in at least 1 eye and bilateral blindness from glaucoma were 26.5% and 5.5%, respectively, after 10 years, and 38.1% and 13.5% at 20 years.**
• CONCLUSIONS: **Approximately 1 out of 6 glaucoma patients was bilaterally blind from glaucoma at the last visit. Median duration of bilateral blindness was 2 years. (Am J Ophthalmol 2013;156:724–730. © 2013 The Authors. Published by Elsevier Inc.** Open access under CC BY-NC-ND license.

THE RISK OF VISUAL DISABILITY FROM GLAUCOMA IS probably the most important question for a newly diagnosed glaucoma patient. It is well known that open-angle glaucoma (OAG) is a major reason for blindness, and that glaucoma is the second most important reason for blindness worldwide.[1] Nevertheless, the risk of blindness attributable to glaucoma for a white patient with OAG is often assumed to be small.[2,3] Several studies have addressed the risk of glaucoma blindness,[3–7] but only few published studies followed glaucoma patients until death.[8–10]

The average duration with a glaucoma diagnosis has been estimated to be approximately 13 years in white patients,[11] but little is known about the duration of blindness in glaucoma patients.

We have access to data on a large and representative part of all diagnosed glaucoma patients in our catchment area (population 305 000). This gave us the opportunity to study the lifetime risk of low vision and blindness in patients with open-angle glaucoma as well as the time with visual impairment from glaucoma.

METHODS

THIS RETROSPECTIVE STUDY WAS CONDUCTED FOLLOWING the tenets of the Declaration of Helsinki. The Regional Ethical Review Board of Lund, Sweden approved the retrospective chart review and usage of the acquired data.

Approximately three-quarters of all known glaucoma patients in Malmö are diagnosed and followed at Skåne University Hospital, Malmö. Patients with permanent visual disability are referred to 1 institution: the Habilitation and Assistive Technology Service in Malmö. We used the patient administrative systems of both the hospital and the Habilitation and Assistive Technology Service in Malmö to identify patients with manifest glaucoma with visual field loss. Patients who died between January 1, 2006 and June 30, 2010 (according to the national tax registration system) were then included. The records of all identified patients were reviewed and all relevant data were noted.

Eligible patients had to have OAG, primary open-angle glaucoma (POAG), or exfoliative glaucoma (PEXG). Patients with other types of glaucoma were not included. Records of visual acuity (VA) and/or visual field (VF) examination during the last 3 years before patients' deaths were required. Patients who were blind at the time of the last visit were included even if the time between the last visit and death exceeded 3 years.

Patients included in the study were divided into 2 groups: the first group included patients who had been followed at Skåne University Hospital already from the start, giving us access to visual acuity, visual field status, and age at the time of diagnosis. Patients in the other group were initially diagnosed outside Skåne University Hospital and referred to our outpatient department only later during follow-up. Complete data (including visual acuity and visual field status)

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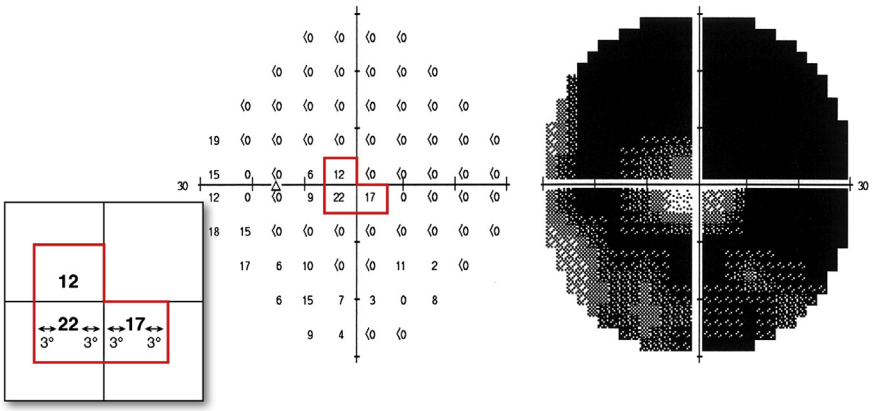

FIGURE 1. Determination of low vision and blindness based on visual field status. The calculation of the widest diameter of the remaining central visual field was done as follows: A pseudoisopter (red line) is drawn midway between points with threshold sensitivity values ≥10 dB and points with sensitivities < 10 dB, indicating the remaining visual field. The space between the pseudoisopter and test points is 3 degrees and the distance between each test point is 6 degrees. The widest diameter of the remaining visual field is calculated by using the pseudoisopter. This field is constricted to 12 degrees around the point of fixation.

for these patients were available from the first examination at the hospital. Here, we refer to the groups as the Data at Diagnosis and the Follow-up Only group, respectively.

For each included patient we recorded sex, age at death, and time between last visit and death. For patients in the Data at Diagnosis group (423/592, 71.5%) we also noted type of glaucoma (POAG or PEXG), age at diagnosis, and years with a glaucoma diagnosis. The presence of exfoliation syndrome (PEX) was recorded if noted at the time of diagnosis or up to 1 year later. In addition, all available data were reviewed to clarify if PEX had been documented in eyes that had undergone cataract surgery before the glaucoma diagnosis was established.

A diagnosis of glaucoma required that at least 1 eye: (1) showed a repeatable visual field defect (VFD) consistent with glaucoma and not explained by other causes; or (2) had only 1 visual field test but with a VFD consistent with glaucoma and a corresponding optic disc abnormality; or (3) was already blind (visual acuity <0.05) at time of diagnosis and had a record of a totally cupped glaucomatous optic disc.

Patients were excluded if other disease made it impossible to establish a glaucoma diagnosis with certainty or to determine whether the visual field showed glaucomatous field loss or not (eg, patients with optic disc drusen or endocrine ophthalmopathy).

Patients were routinely followed with standard automated perimetry using the Humphrey perimeter (Carl Zeiss Meditec, Dublin, California, USA) 30-2 or 24-2 Full-Threshold or SITA programs. Visual field defects were defined as glaucomatous if they showed a pattern consistent with glaucoma (eg, a nasal step or a paracentral or arcuate defect). In addition, the Glaucoma Hemifield Test (GHT) had to be classified as "borderline" or "outside normal limits." Visual fields were considered reliable if false-positive responses were fewer than 15% and a clear blind spot could be seen in the visual field printouts (threshold value <10 dB). Nonglaucomatous fellow eyes without VF measurements at diagnosis were set to a mean deviation (MD) value of 0 dB, indicating a normal visual field.

We registered best-corrected VA and the remaining visual field by measuring the widest diameter of the central visual field at the time of diagnosis or up to 1 year after diagnosis (in the Data at Diagnosis group only) and at the last visit before death (in all included patients). We used the recommendations of the United States Social Security Administration[12]: a pseudoisopter was drawn by hand midway between points with threshold sensitivity values ≥10 dB and those with values <10 dB on the Humphrey Field Analyzer numerical dB printout (Figure 1). The mean value was used if 2 threshold values were measured at a given test point location. This pseudoisopter was used to measure the widest diameter of the remaining central visual field, to assess if an eye was blind or had low vision.

Using the World Health Organization (WHO) criteria for low vision (0.05 [20/400] ≤ VA < 0.3 [20/60] and/or 10 degrees ≤ central VF < 20 degrees) and blindness (VA <0.05 [20/400] and/or central VF <10 degrees), we defined the following 4 categories of low vision and blindness with glaucoma as the main cause: (1) unilateral low vision: patients with low vision in 1 eye; (2) bilateral low vision: patients with low vision in the best eye; (3) unilateral blindness: patients blind in 1 eye; (4) bilateral blindness: patients with both eyes blind, mainly caused by glaucoma in at least 1 eye.

The cause of visual disability was determined by reviewing patient charts and analyzing the information in relation to the VF appearance. In most patients the main reason for visual disability was clear. In a few eyes it was impossible to

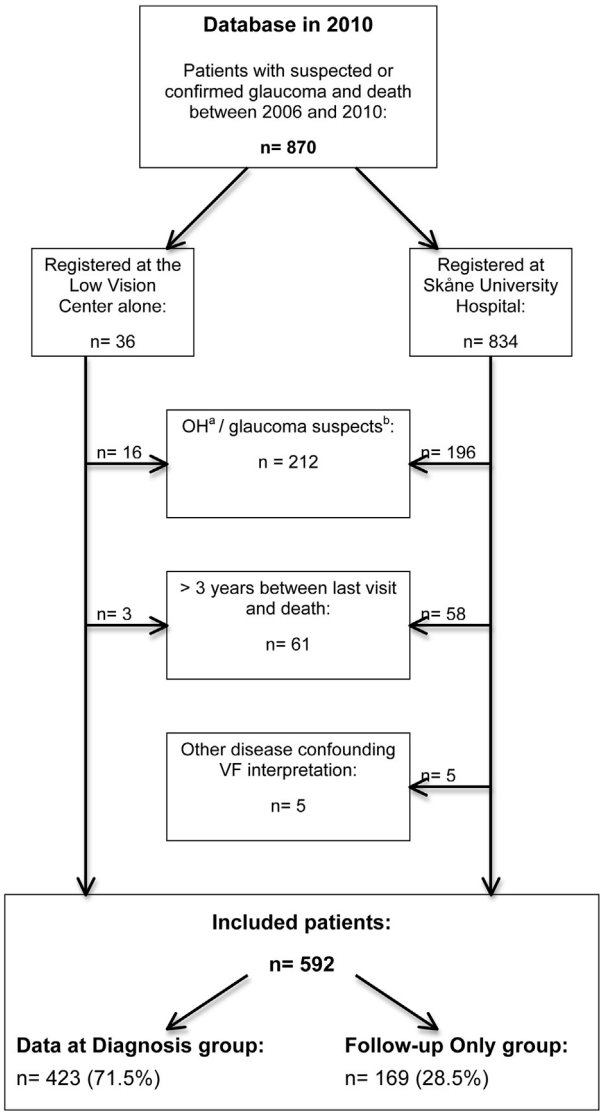

FIGURE 2. Patient flowchart showing the procedure of identification of patients with open-angle glaucoma. Using the patient administration system of the Skåne University Hospital identified most glaucoma patients included in the study. Patients registered only at the Low Vision Center (Habilitation and Assistive Technology Services) were followed by private ophthalmologists alone. Included glaucoma patients were divided into 2 groups: (1) patients with visual field data available at time of diagnosis (Data at Diagnosis group); and (2) patients with visual field data available only from follow-up but not from the time of diagnosis (Follow-up Only group). VF = visual field; OH = ocular hypertension. [a]Elevated intraocular pressure with normal visual field and normal optic disc. [b]Description of a glaucomatous optic disc defect in the records but no visual field measurement available or visual field defect not concordant with the disc description.

determine a single cause of visual disability. Then we recorded a combination of causes.

The date of the glaucoma diagnosis was set to the date of the first reliable VF showing a glaucomatous defect. The time for low vision or blindness was the first visit when the Humphrey field was centrally constricted to less than 20 degrees or 10 degrees, respectively, or when VA was permanently reduced to below 0.3 (20/60) or 0.05 (20/400), respectively. Even in those few patients who had missed many consecutive visits during follow-up, all available data on visual function were analyzed as of the date from the next visit.

• **STATISTICAL ANALYSES:** Time with glaucoma blindness and the final outcomes in terms of low vision and blindness from glaucoma were determined in all included patients.

Cumulative incidence of blindness and time with diagnosed glaucoma were calculated in the Data at Diagnosis group. We chose to calculate cumulative incidences with a competing risk method.[13] Contrary to the Kaplan-Meier method, the competing risk method does not "censor" individuals with competing risks. Thus, the probability of an event-free survival calculated with the competing risk method is a conditional probability, which takes both the event and the competing risks into account. In our analysis, blindness attributable to reasons other than glaucoma or death without blindness were modeled as competing risk events. Annual incidence rates were calculated setting all "study" events (blindness attributable to glaucoma) and all competing events to the time point just prior to the end of the annual period. In addition, cumulative incidences for blindness in at least 1 eye and bilateral blindness were calculated with the Kaplan-Meier method[14] in order to be able to compare our results with previously published results.

The Pearson χ^2 test was used to compare the rates of low vision and blindness in the Data at Diagnosis and Follow-up Only groups. All statistical calculations were performed with SPSS version 19.0 (SPSS Inc, Chicago, Illinois, USA). Statistical significance was set to $P < .05$.

RESULTS

FIVE HUNDRED AND NINETY-TWO OF 662 PATIENTS (89.4%) with manifest glaucoma with visual field loss met the inclusion criteria (Figure 2). Three hundred and sixty-seven (62.0%) were female and 372 patients (62.8%) had glaucoma in both eyes. Seventeen of all included patients (2.9%) were registered in the administration system of the Habilitation and Assistive Technology Service only. Median time between last visit and death was 8 months (interquartile range 3-16 months). Median age at death was 87 years (range 50-103 years).

There were 423 patients in the Data at Diagnosis group (71.5%). In those patients mean age at diagnosis was 74.0 ± 7.9 years, ranging from 46-95 years. Exfoliative glaucoma was found in at least 1 eye in 170 patients (40.2%). Average perimetric MD at diagnosis was −5.59 ± 5.69 dB

TABLE. Numbers of Low Vision and Blindness From Glaucoma at Last Visit for (1) Patients With Visual Field Data Available at Diagnosis, (2) Patients With Visual Field Data Available Only From Follow-up, and (3) All Included Patients

	All Patients (n = 592) n (%)	Follow-up Only Group (n = 169) n (%)	Data at Diagnosis Group (n = 423) n (%)
Unilateral low vision			
OAG	52 (8.8)	13 (7.7)	39 (9.2)
Bilateral low vision			
OAG + OAG	7 (1.2)	2 (1.2)	5 (1.2)
OAG + other cause	5 (0.9)	1 (0.6)	4 (0.9)
In total:	12 (2.0)	3 (1.8)	9 (2.1)
Unilateral blindness			
OAG	153 (25.8)	51 (30.2)	102 (24.1)
Bilateral blindness			
OAG + OAG	67 (11.3)	22 (13.0)	45 (10.6)
OAG + other cause	30 (5.1)	10[a] (5.9)	20[b] (4.7)
In total	97 (16.4)	32 (18.9)	65 (15.4)

OAG = open-angle glaucoma.

The Data at Diagnosis group represents patients with visual field data available at the time of diagnosis. The Follow-up Only group represents patients diagnosed outside and later referred to the Skåne University Hospital, and for whom the first visual field data were available after the time of diagnosis.

[a]One eye blind from: age-related macular degeneration in 5 patients; secondary glaucoma in 2 patients; a combination of glaucoma and cataract in 1 patient; a combination of glaucoma and myopia in 1 patient; central venous occlusion in 1 patient.

[b]One eye blind from: age-related macular degeneration in 6 patients; a combination of glaucoma and age-related macular degeneration in 5 patients; trauma in 2 patients; retinal detachment in 2 patients; central venous occlusion in 2 patients; secondary glaucoma in 2 patients; cerebral vascular accident in 1 patient.

and −11.83 ± 8.18 dB in the better and the worse eye, respectively. Median VA at time of diagnosis was 0.8 (20/25), ranging from no light perception to 1.00 (20/20), in the perimetrically better eye and 0.8 (20/25), ranging from no light perception to 1.25 (20/16), in the perimetrically worse eye. Untreated mean intraocular pressure (IOP) value in all glaucomatous eyes at time of diagnosis was 27.2 ± 8.8 mm Hg.

Numbers of patients with low vision and blindness from glaucoma at the last visit are shown in the Table. At the last visit, 42.2% (250 of 592 patients) of all patients were blind from glaucoma in at least 1 eye and 16.4% in both eyes. Other reasons for unilateral blindness were age-related macular degeneration (AMD) (26 patients), a combination of cataract and other disease (10 patients), and other causes (32 patients). Seventeen patients were bilaterally blind because of reasons other than glaucoma (16 from AMD, 1 patient from other reason). A combination of causes for blindness was found in 1 eye of 7 blind patients (Table). There was no statistically significant difference in the frequencies of visual impairment at the last visit when comparing the Data at Diagnosis group and the Follow-up Only group (Table, $P = .260$). In patients who developed blindness attributable to glaucoma, the median time with bilateral blindness was 2 years (<1-13) (mean 3.0 ± 3.1). Patients who became bilaterally blind from glaucoma did so at a median age of 86 years (range 66-98; mean 85.7 ± 6.1). Only 13 patients (13.5% of blind patients and 2.2% of all patients) became blind before the age of 80 years.

The median duration with diagnosed glaucoma was 12 years (<1-29) (mean 11.2 ± 6.6), and 74.7% (316 of 423 patients) of patients had their glaucoma diagnosis for more than 6 years.

The cumulative incidence for blindness in at least 1 eye and bilateral blindness from glaucoma was 26.5% and 5.5%, respectively, at 10 years and 38.1% and 13.5%, respectively, at 20 years after diagnosis (Figure 3, Top left and Bottom left). The corresponding cumulative incidences for blindness caused by other reason were 0.7% and 0.7%, respectively, at 10 years and 2.4% and 2.6%, respectively, at 20 years (Figure 3, Top left and Bottom left). The Kaplan-Meier estimates for blindness in at least 1 eye caused by glaucoma were 33.1% at 10 years and 73.2% at 20 years (Figure 3, Top right) and 8.6% at 10 years and 42.7% at 20 years for bilateral blindness from glaucoma (Figure 3, Bottom right).

DISCUSSION

IN THIS STUDY OF LIFETIME RISK FOR BLINDNESS A LARGE proportion of patients (42.2%) were blind from glaucoma in at least 1 eye at the last hospital or Habilitation and Assistive Technology Service visit, and 16.4% were bilaterally blind from glaucoma. The cumulative risk for unilateral and bilateral blindness from glaucoma was considerable and many blind patients were blind for more than 3 years. Patients included in the cumulative risk analyses (Data at Diagnosis group) were diagnosed in 1980 or later, and 66% were diagnosed after 1993. Hence, they were likely to have benefited from the improvements in glaucoma management occurring over the last 30 years.

One strength of the current study is the relatively large sample size and the fact that visual function was followed as long as possible, on average to less than 1 year before death. By including only dead glaucoma patients we had access to almost complete follow-up data for all patients, making it easy to determine the "final" percentage of blind eyes and patients. Another strength is that we used the registration system of the Habilitation and Assistive Technology Service in addition to the patient administration system of our hospital to identify potentially eligible patients, allowing us to include visually impaired glaucoma

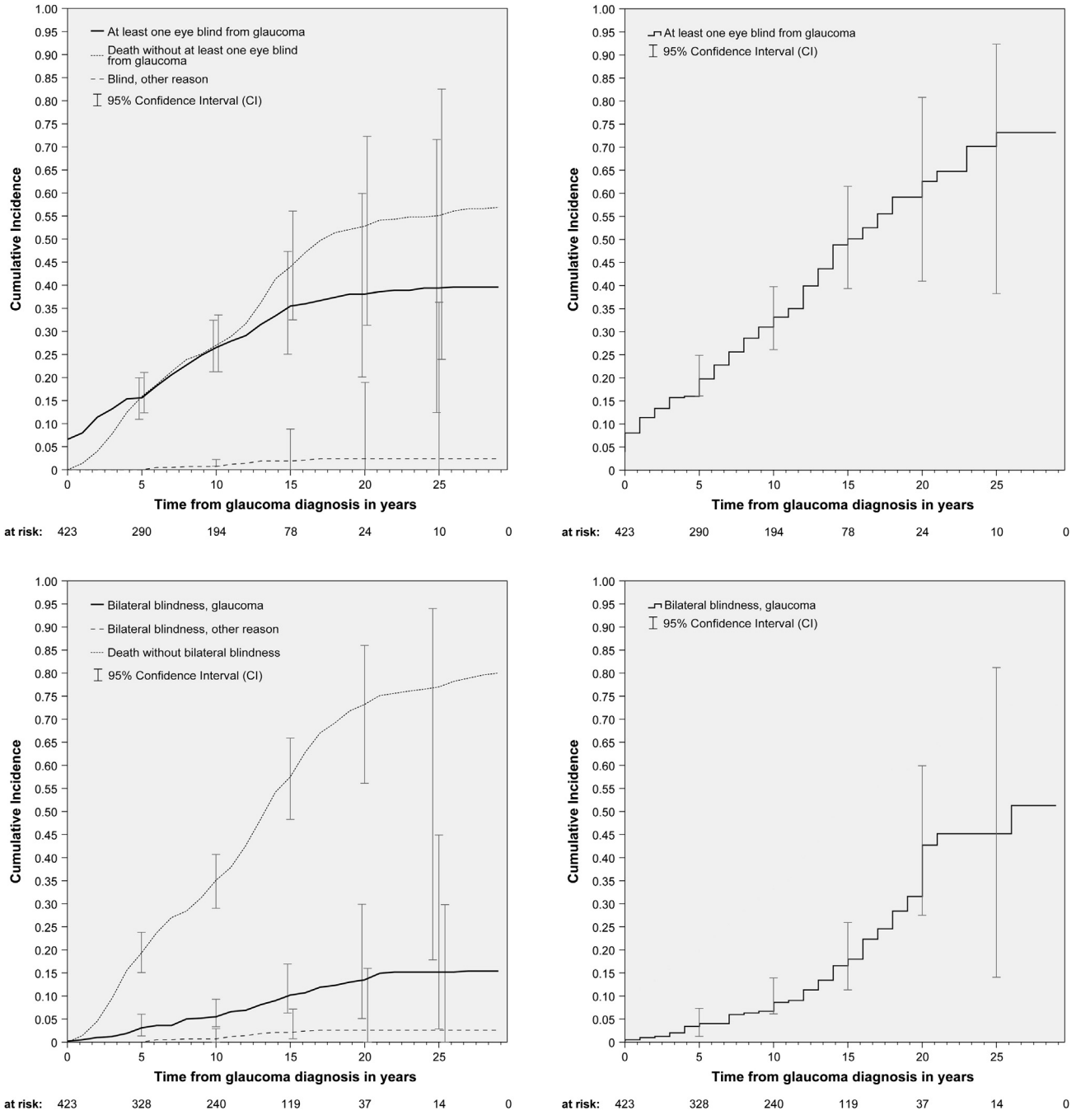

FIGURE 3. Cumulative incidence rates for unilateral and bilateral blindness caused by glaucoma patients from the Data at Diagnosis group (n = 423). (Top left) Cumulative incidence rates of unilateral blindness caused by glaucoma, blindness caused by other reason, and death without unilateral blindness. (Top right) Kaplan-Meier estimates for unilateral blindness caused by glaucoma. (Bottom left) Cumulative incidence rates of bilateral blindness caused by glaucoma, blindness caused by other reason, and death without blindness. (Bottom right) Kaplan-Meier estimates for bilateral blindness caused by glaucoma.

patients who may have sought help from social services rather than ophthalmologists. People living in our catchment area have the opportunity to access care at our department without mandatory referral from another ophthalmologist. Most glaucoma patients in our catchment area are seen at our hospital. Patients initially diagnosed and followed by one of the few private ophthalmologists working in the city are often referred to our clinic during follow-up for second opinion, laser treatment, or surgery. This, and the fact that the Habilitation and Assistive

Technology Service low vision center is the sole unit for referral in the area, makes it likely that few blind patients have been missed.

The exact number of glaucoma patients in our catchment area who are followed by private ophthalmologists alone is unknown, however. We therefore could have overestimated the rates of visually disabled glaucoma patients by including glaucoma patients registered at the Habilitation and Assistive Technology Service. However, we found only 3 patients who were blind from glaucoma who were registered at the Habilitation and Assistive Technology Service but not at the patient administration system of our hospital. On the other hand, we found that nearly 29% (49/170) of all patients who were visually impaired from glaucoma never had been in contact with the Habilitation and Assistive Technology Service. This is a considerable proportion, albeit lower than earlier reported.[15,16] We may, therefore, have missed some visually impaired glaucoma patients who neither had visited our department nor had been in contact with the Habilitation and Assistive Technology Service. In 61 patients, time between last visit and death exceeded 3 years. We cannot determine whether the exclusion of these patients has significantly altered the results.

The retrospective design of this study results in some limitations. In a few included patients (n = 25) only 1 reliable VF was available, mainly because the initial VF already showed an advanced visual field defect and therefore those eyes were not retested, or because the patient died shortly after the diagnosis. In all those cases the VF showed a typical glaucomatous defect and the optic disk description was in agreement with the VF appearance.

We chose to analyze the rates of low vision and blindness in all included patients (n = 592). In more than 70% (n = 423) of our study population we had access to patient age, visual acuity, and visual fields as of the time of diagnosis (Data at Diagnosis group), making it possible to calculate the cumulative incidence of blindness from glaucoma in this group only. We had access to the exact date of death, but set the date of blindness to the date of the visit when a patient satisfied blindness criteria. Therefore the time to blindness could have been somewhat overestimated, particularly for patients who had missed many consecutive visits during follow-up. However, the latter was the case for only 2 unilaterally blind patients.

The proportions of patients with low vision and blindness were similar in the 2 groups, however, with 18.9% bilaterally blind patients in the Follow-up Only group vs 15.4% bilaterally blind patients in the Data at Diagnosis group. This makes us believe that the results can be generalized for the catchment area, and perhaps to northern Europe. The study population contained predominantly white subjects. Therefore the results cannot be generalized to other populations with different ethnicity.

In most Western countries approximately 50% of all glaucoma patients are unaware of their disease,[17–19] and hence many glaucoma patients die unaware of their disease. In Malmö later stages of visual field loss were considerably more common in clinically diagnosed patients than in glaucoma patients identified through population screening.[20] It must be considered likely that most glaucoma patients with advanced disease leading to blindness or low vision will seek medical help. Because of these factors, the risks of impairment given here are valid for diagnosed glaucoma patients only; the risk of blindness including undiagnosed patients must be considerably smaller.

To our knowledge, there are only 3 published studies analyzing lifetime blindness from OAG. A Finnish study performed by Forsman and associates[8] showed results similar to ours but with a smaller sample size. In this study 12% of patients with manifest glaucoma were blind from glaucoma at the time of the last visit, a result that is comparable to ours. Our rates of low vision and blindness are considerably higher than those reported by Ang and Eke[9] (6.6% with partial sight certification, 0% blind). Our study population was nearly 4 years older at the time of the last visit than that of Ang and Eke, and our follow-up time was also longer (11.2 vs 7.4 years). Both of these factors may contribute to higher numbers of visually disabled patients in Malmö. Goh and associates[10] also found lower rates of visual disability, but defined low vision and blindness by VA alone, which leads to falsely low rates. In accordance with findings in several other studies,[4,8,21,22] approximately 35% (33 of 97) of all blind patients would have been missed if impairment had been based on VA alone.

Over the last 15 years some longitudinal studies have reported rates of blindness caused by OAG at different points in time after diagnosis. Hattenhauer and associates[4] found a 54% risk for unilateral blindness and a 22% risk for bilateral blindness after 20 years in treated patients with "classic glaucoma" (defined as patients with field loss). The estimated risks for blindness in 1 or both eyes 10 years after diagnosis were 26% and 7%, respectively. Kwon and associates[5] reported a cumulative rate of unilateral blindness for glaucoma patients followed with Goldmann perimetry (40 patients) of 19% at 22 years. More recently, Chen[3] analyzed 186 patients with open-angle glaucoma diagnosed in 1975 or later and found a 14.6% risk for unilateral blindness and a 6.4% risk for bilateral blindness after 15 years. Considering that improved methods both for diagnosis and for treatment have certainly become available after the late 1970s, one would expect lower rates of low vision and blindness in our study compared to those of Hattenhauer and perhaps similar numbers to those of Chen. Instead, our results are similar to those found in the Olmsted population[4] when comparing our cumulative incidence rates calculated with the Kaplan-Meier method. On the other hand, impairment rates in the present study calculated by the competing risk method are approximately twice as high as those reported by Chen.

One explanation is that we followed patients to death, in contrast to Chen. In our population blindness almost always occurred at high ages and only 13 patients became blind before 80 years of age. We also had a higher percentage of patients with exfoliative glaucoma in our study population (40.2%) than both Hattenhauer and associates (8.5%) and Chen (14 %), which could contribute to the high rates of blindness in our study.

The mean duration of diagnosed disease of 11.2 years in the current study is similar to the estimate of 12.8 years reported in 1997 by Quigley and Vitale.[11] Mean duration of blindness was only 3 years. Fuchs and associates[23] found that glaucoma patients' mean time as members of the Danish Association of the Blind (DAB) from admission to death (indicating time with blindness) decreased over time from about 16 years in 1960 to approximately 6 years in 1970. We have been unable to find other population-based published data on duration with visual disability in glaucoma.

Thus, we found that approximately 1 out of 6 glaucoma patients was bilaterally blind at the last visit, while more than 40% were blind in at least 1 eye. Blindness mostly occurred at late ages, and the great majority of bilaterally blind patients were older than 80 years when the best eye became blind.

Life expectancy has increased considerably during the last 50 years, by 10 years in the United States, and is expected to increase further. With longer life expectancy, glaucoma patients will have the disease for a longer time and it is possible that the lifetime risk of glaucoma blindness may increase even further.

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